Strategies for the introduction of JE vaccine into routine immunization

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Important Update

- Bad press in India
- No deaths or serious adverse events have been associated with the live attenuated vaccine used in India
- Great deal of misinformation
- Highlights one of the challenges of working in the developing world (particularly India)
- I would be happy to talk about any of these reports with anyone who has any questions

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Overview

- Brief introduction into JE epidemiology
- Discuss the barriers to JE control
- Introduce the JE project
- Review the strategy for vaccine introduction
- Discuss recent success in India and Nepal

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Age groups affected by JE

- Children 1 to 15 years of age are mainly affected in endemic areas.
- But people of any age can be infected. Adult infection most often occurs in areas where the disease is newly introduced.

Photo credit: Carib Nelson, PATH

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Japanese Encephalitis

- Leading cause of viral encephalitis in Asia
- Leading neuorlogic infection in Asia
- 50,000 cases annually reported throughout Asia
  - severely under-reported
- 10,000 -15,000 deaths annually (5-35% CFR)
- JE-related disability 30-75%

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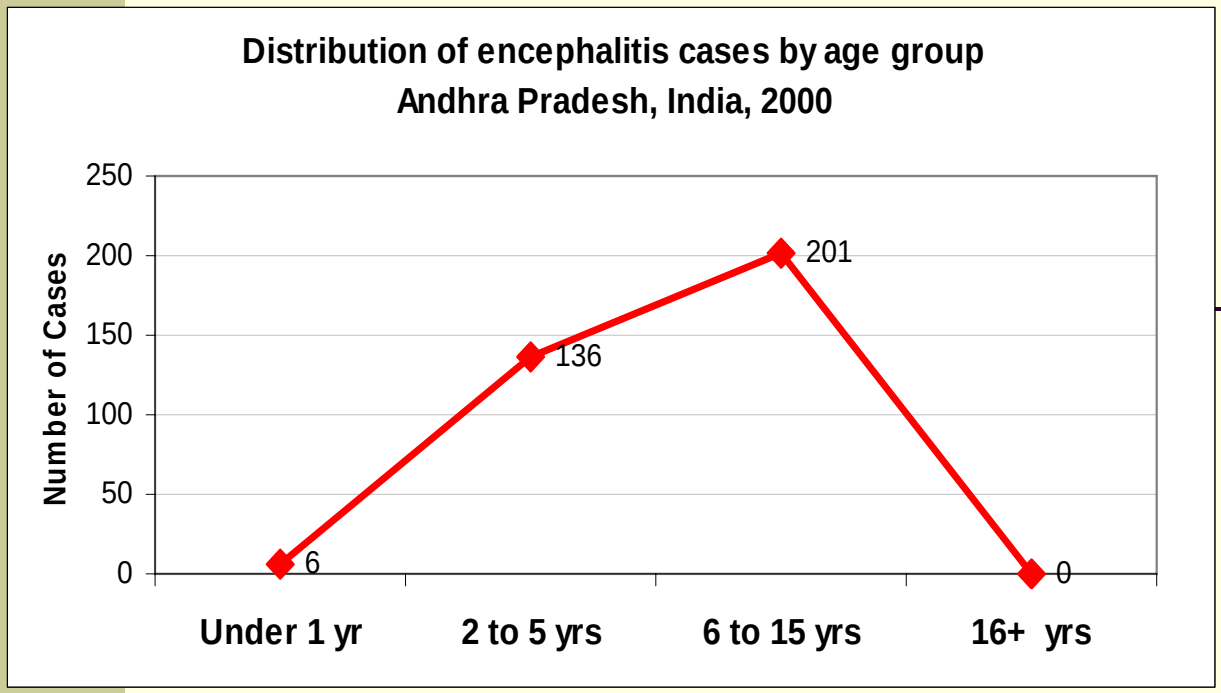
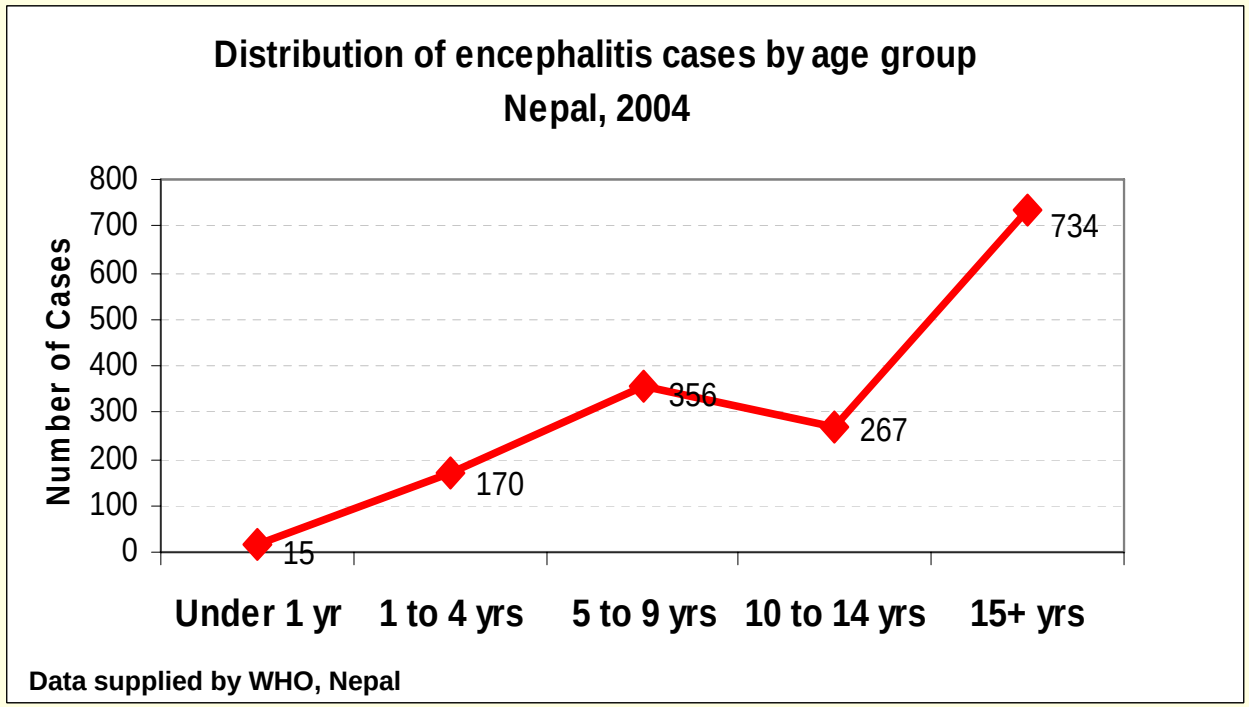


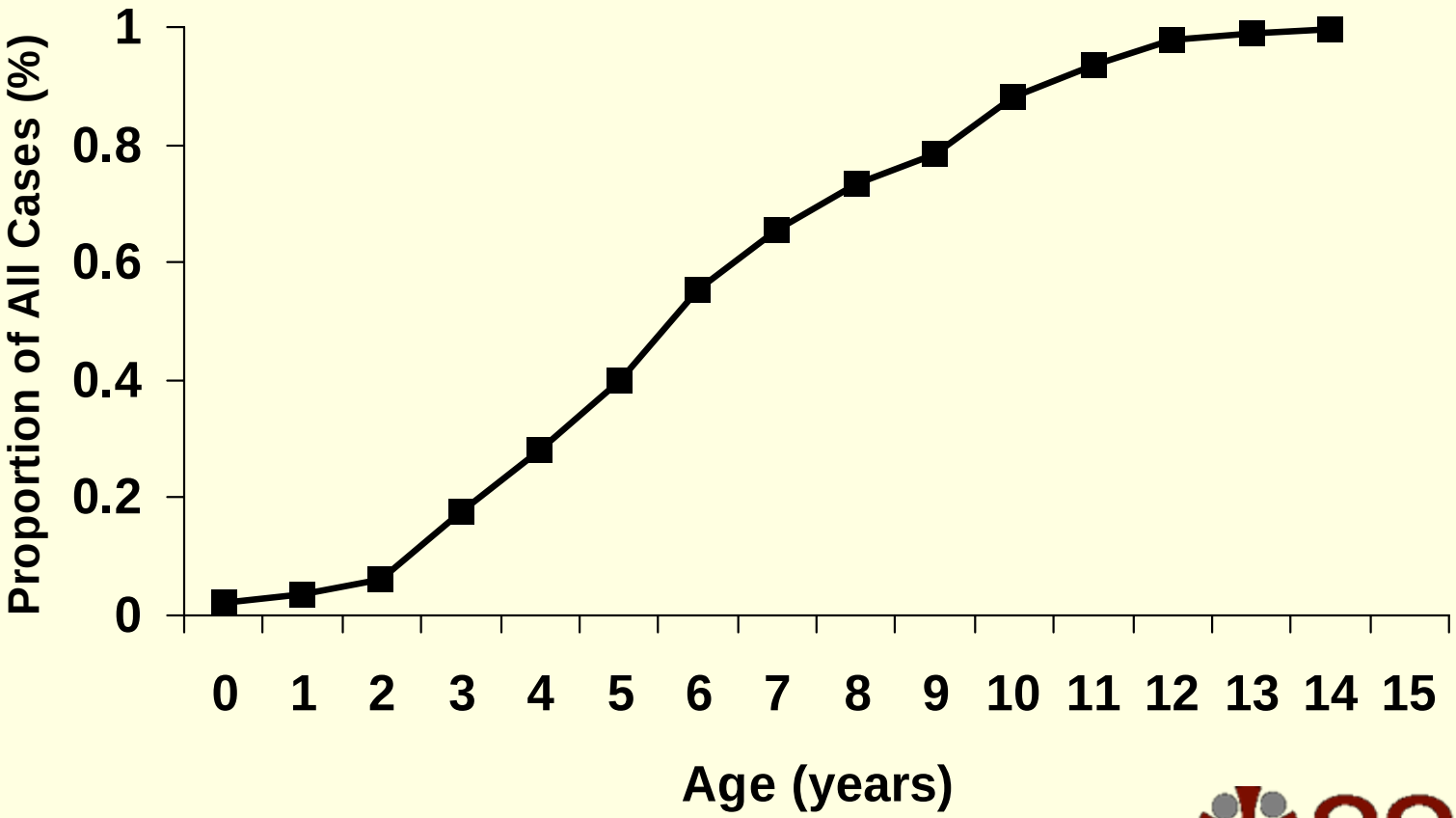
Data supplied by Government of Andhra Pradesh

Different patterns of age distribution of cases



Data supplied by WHO, Nepal

Figure 2: Cumulative Proportion of JE by Age, Andhra Pradesh, 2000



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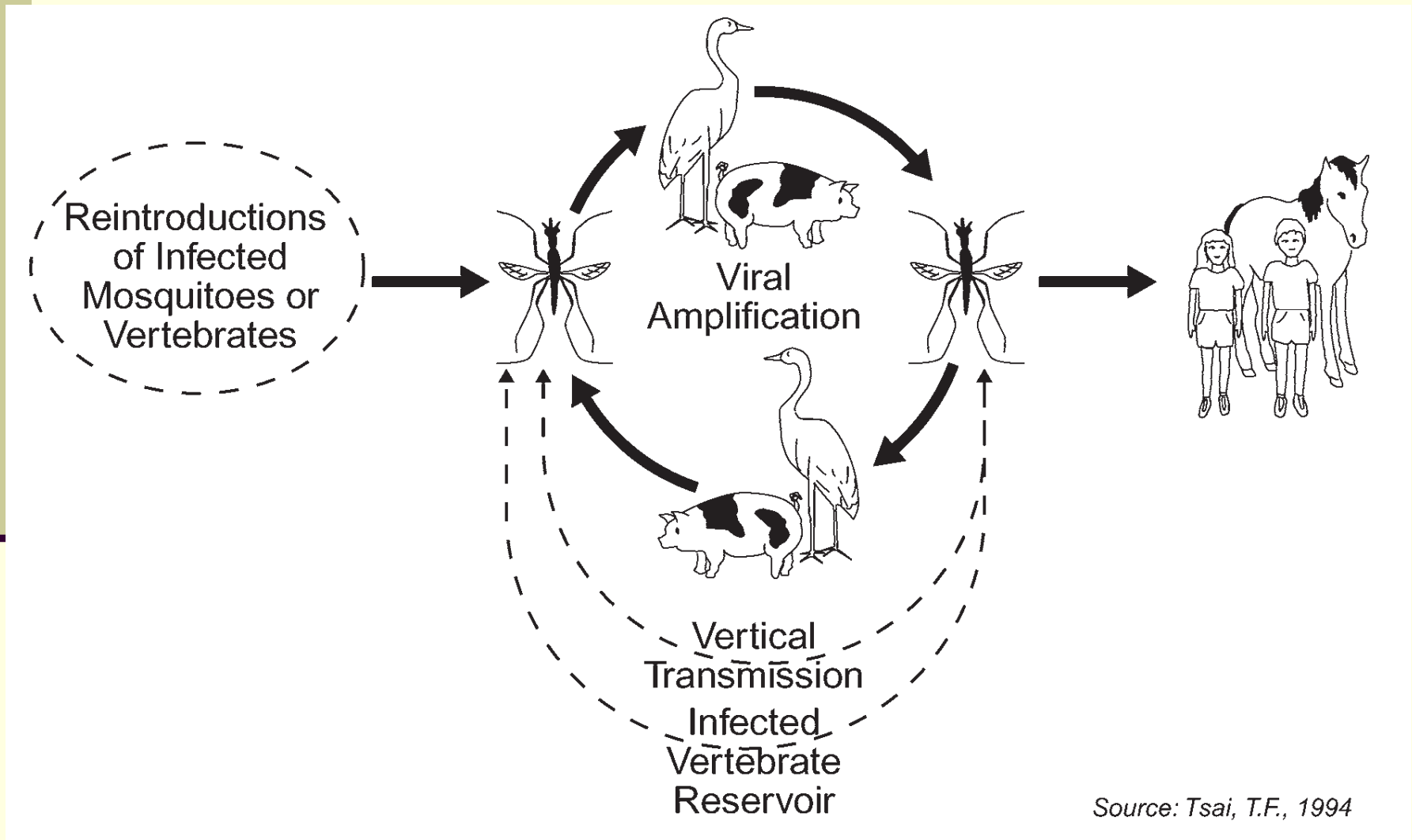
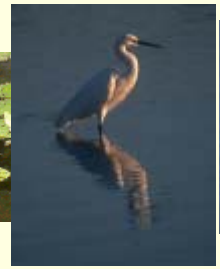
JE Transmission Cycle















Slide from Dr PN Rao
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Barrier 1: Poor recognition

- Surveillance
- Diagnostics

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Under-reporting JE cases

- Poor surveillance
- Diagnostics not easily available

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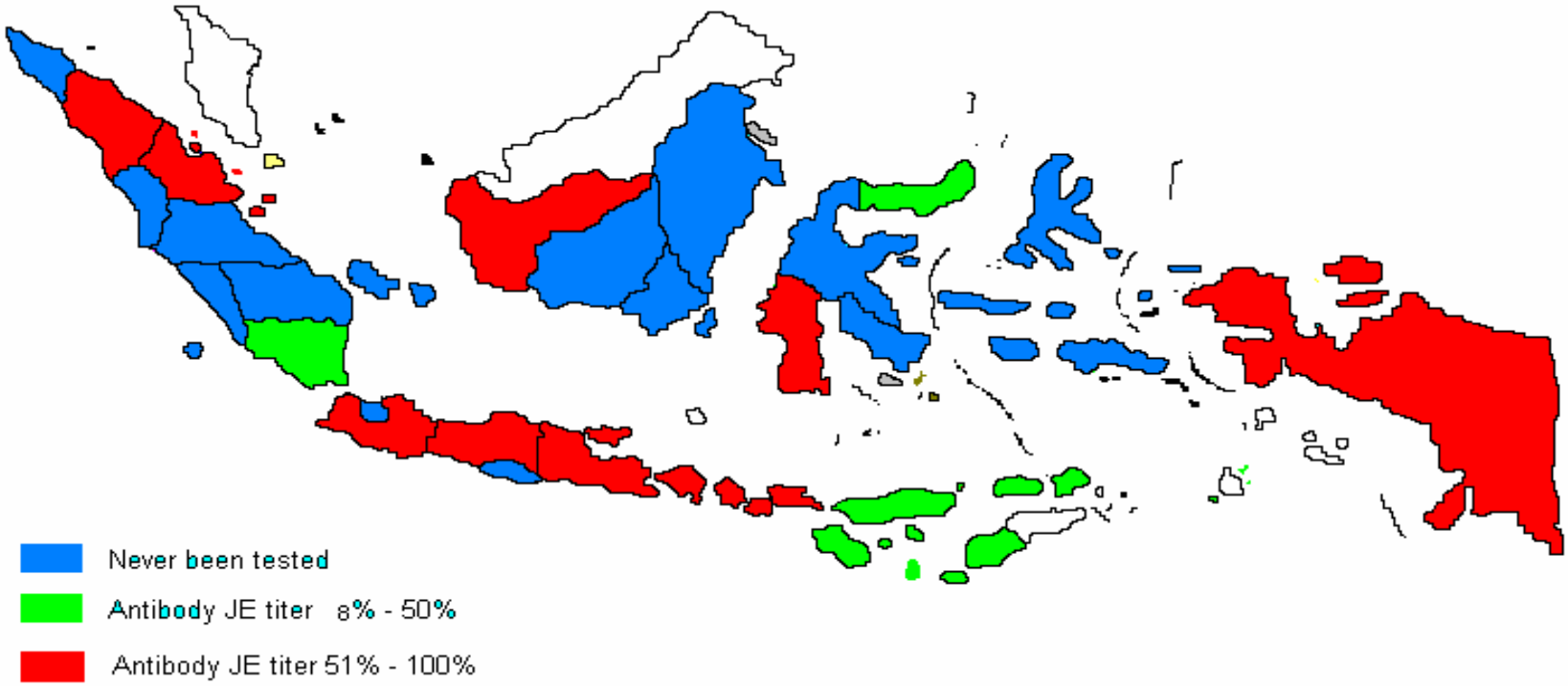
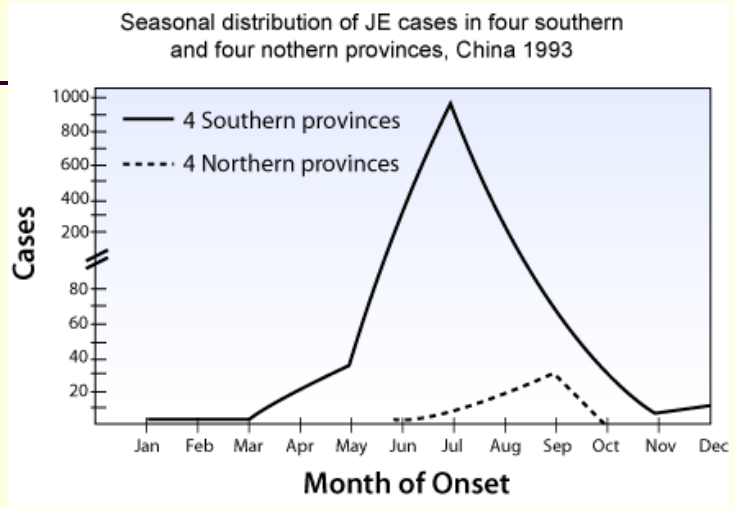
PRESENTAGE JE POSITIVE SPECIMENS IN HUMAN
IN INDONESIA, 1993 - 2000



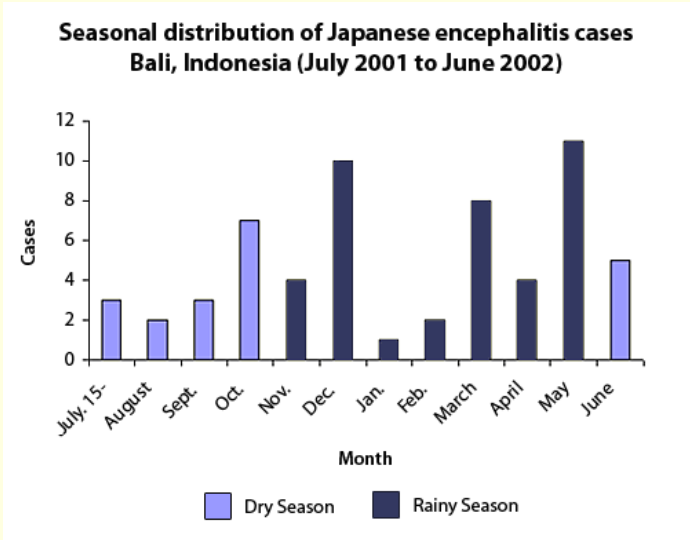
Two patterns of transmission of JE

JE may be spread:

1. Seasonal, called an epidemic pattern (e.g., southern China)



2. Year-round, called an endemic pattern (e.g., Bali, Indonesia)



Data supplied by International Vaccine Institute

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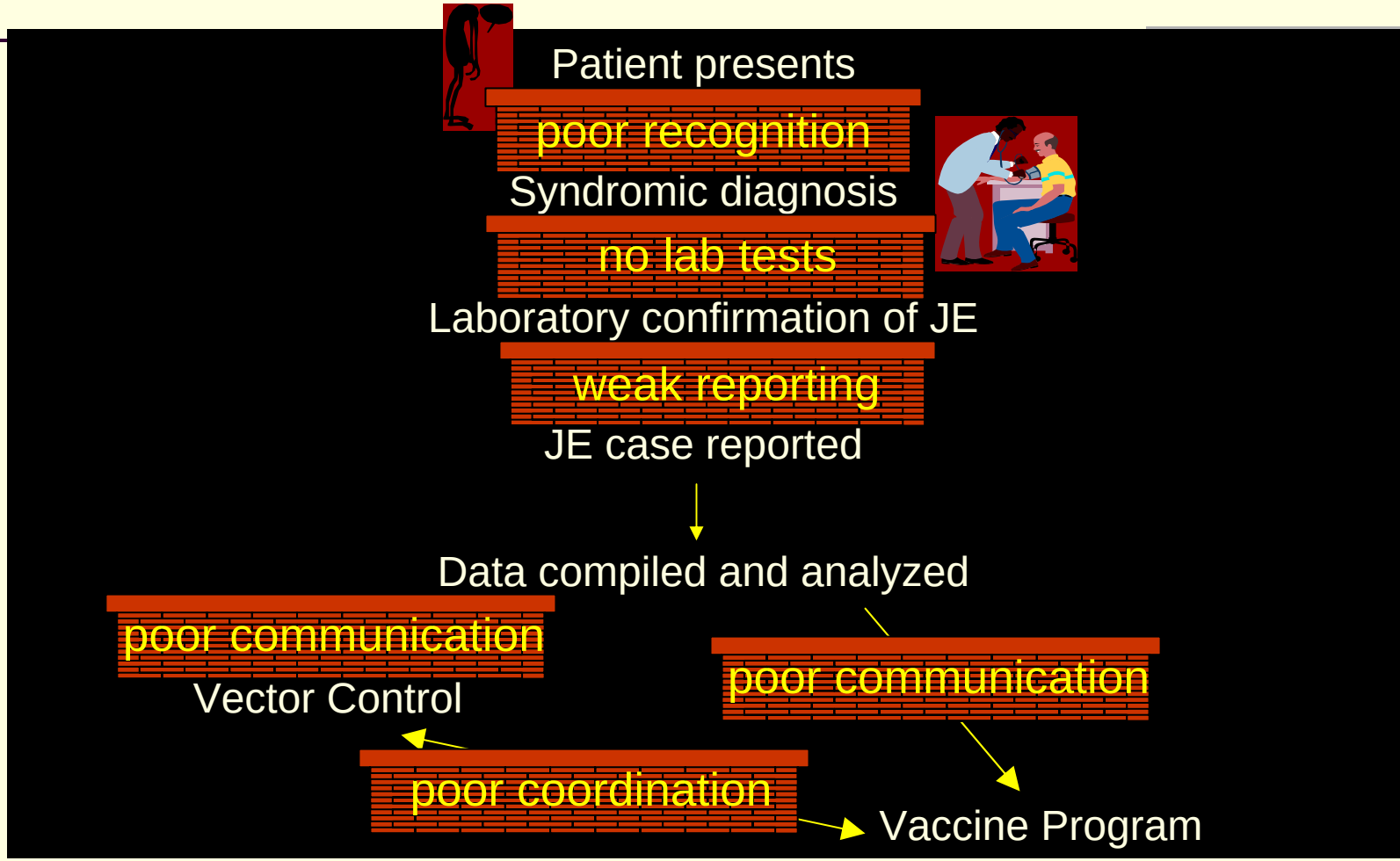
Barriers to Effective JE Control



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Barrier 2: Misconceptions of effective disease control

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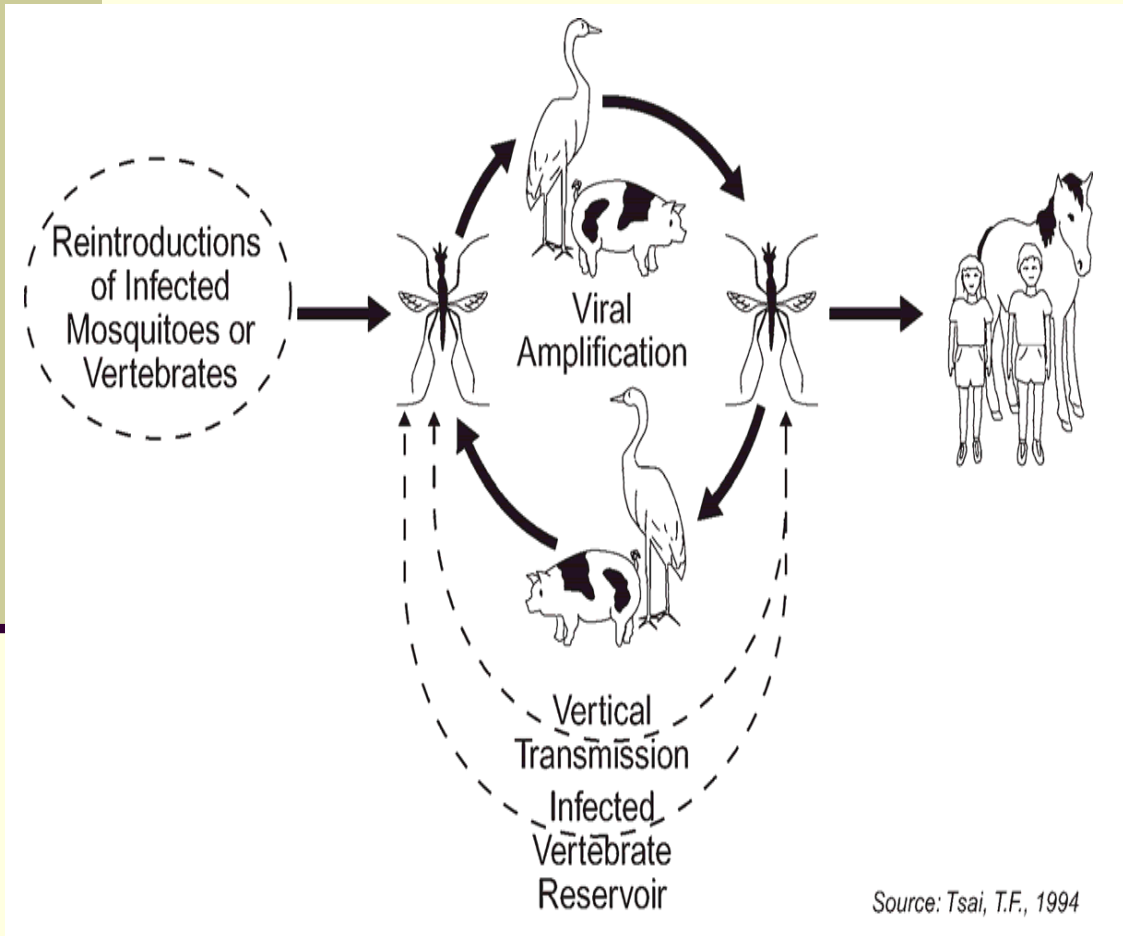
JE transmission cycle and possible control points



Control options

- Mosquito control?
- Pig control?
- Human interventions?

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Mosquito control ?

Photo credit: Julie Jacobson

- Spraying mosquito habitats with insecticide
  - Time consuming, expensive, it is difficult to cover all mosquito habitats, and causes environmental pollution
- Bednets
  - Mosquitoes bite at dusk before people are in bed

NOT THE BEST SOLUTION

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Pig control ?

Photo credit: Susan Hills

- Segregating, slaughtering, or vaccinating pigs
  - Economically not feasible and difficult
  - Other animals, like birds, may also act as amplifying hosts so even if pigs are eliminated JE will not disappear

NOT THE BEST SOLUTION

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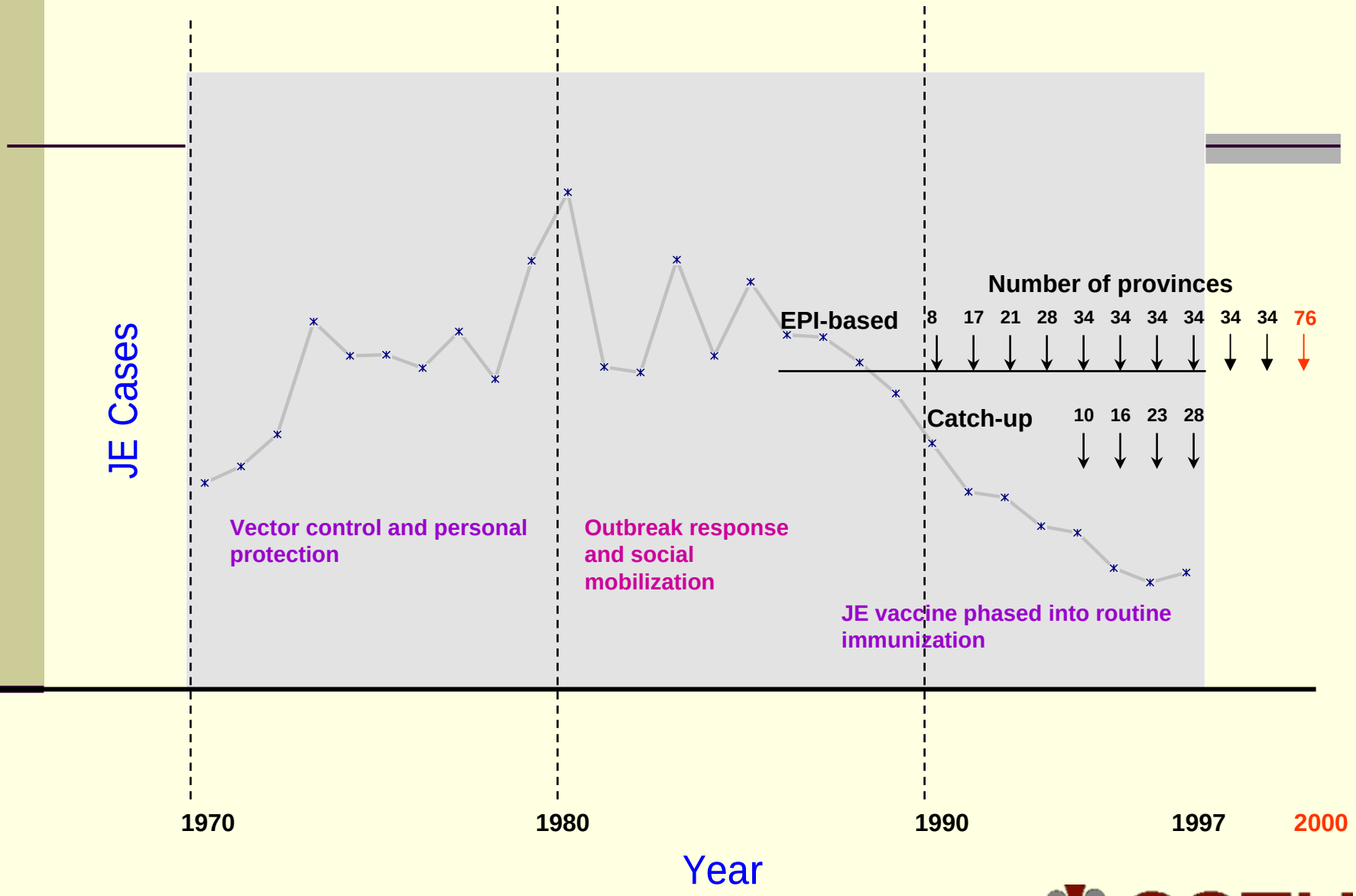
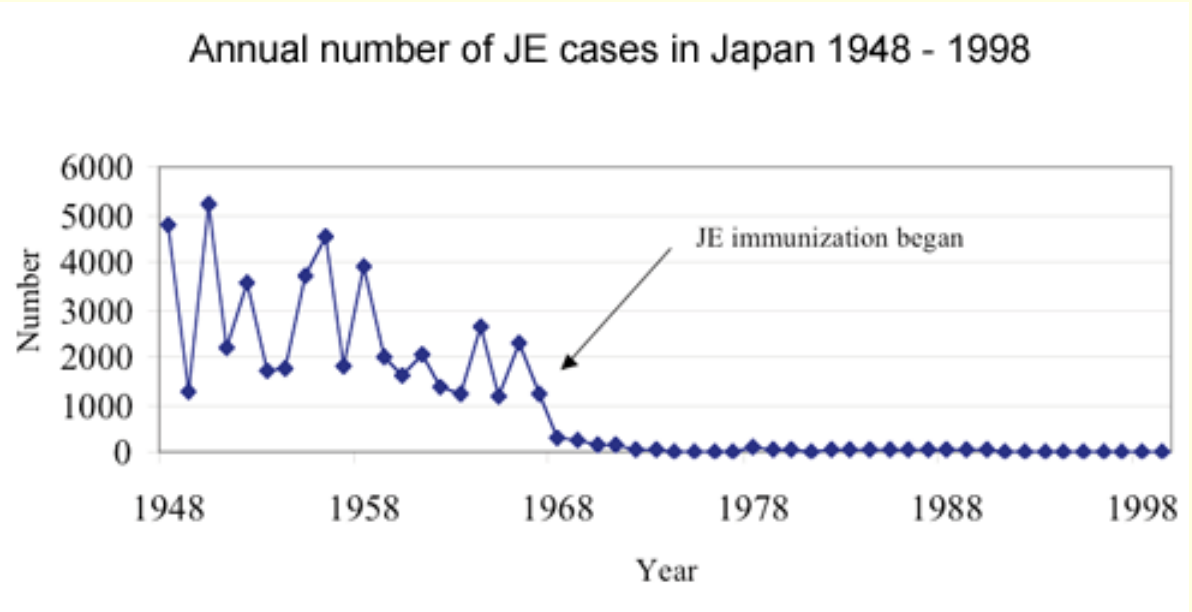
Evolution of JE control in Thailand



Source: Division of GCD, CDC, MOPH

Scientific evidence for JE immunization

There is compelling evidence that human immunization is effective for controlling JE. Studies in Korea and Japan showed >99% reduction in JE cases after immunization.



Source: Igarashi A. "Control of Japanese Encephalitis in Japan: Immunization of humans and animals and vector control" *Current Topics in Microbiology and Immunology* 2002. 267: 139-152.

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Barrier to Vaccination

- Most widely available vaccine mouse brain derived
- Responsible for much of the success to date with JE control
- Unfortunately there are limitations in its use
- Limited supply due to production process
- Expensive to produce
- Difficult schedule
- Side effect profile needs to be considered

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JE Project

- 5-years, funded by the Bill & Melinda Gates Foundation
- Early focus on data for decision-making (surveillance, dissemination, advocacy)
- Vaccine access of product with defined product profile
- Later shift to activities to vaccine introduction

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JE Project Vision

To eliminate clinical JE and avoid the unnecessary death and disability caused by this disease

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JE Project Strategy

To routinely vaccinate all the at-risk population with a safe, efficacious and affordable vaccine

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How do we support country level disease control and decision making?

- Countries must understand their disease burden and develop the will to fight JE
- They need an available, affordable vaccine
- They need increased support from international public health partners
- They need the advice and experience of other countries that have excelled in JE control

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JE Project Goals

1. Improve disease surveillance, including available simple diagnostics
2. Advance an improved vaccine- tailored for the needs of the developing world
3. Introduce and integrate the vaccine
4. Promote JE control nationally and internationally

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Strategy
Country support:

- Support data for decision making and the most cost effective and high impact strategies for JE control in different national settings
- Assist vaccine introduction by providing technical support to countries and partners and distill lessons learned
- Integrate all activities into routine mechanisms so that control program activities are sustained and continued to be expanded by partners

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Surveillance and laboratory work:

- WHO surveillance standards available now
- 2 countries in the past year with new evidence of endemic disease (Indonesia and Bangladesh)
- 3 new commercialized ELISA diagnostic tests in field trials
- WHO lab network under development

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Surveillance

- Indonesia
- Nepal
- Philippines
- Cambodia
- Vietnam
- China
- India

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Strategy
Vaccine development:

- Ensure a safe, efficacious, affordable supply of JE vaccine for use in routine immunization for all endemic countries (particularly GAVI fund eligible countries) that is fundable by international agencies with a reliable supply.

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Vaccine development

- Reviewed available vaccine candidates against the target product profile
- Live attenuated SA 14-14-2 vaccine met the criteria
- Went with an international expert team to review clinical data and inspect facility
- Created a plan to increase access and production capacity
- Negotiated with the Chengdu Institute of Biological Products for a public sector price for vaccine

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Vaccine development
Current situation:

- We have a excellent vaccine with a very good public sector price with a signed agreement.
- Our current plans will address the remaining issues which are adequate supply, fundability (i.e. pre-qualified), and integration into routine EPI.
- Global advisory committee on vaccine safety reviewed the SA 14-14-2 and acknowledged the safety and efficacy data
- Discussing work with additional late stage candidates with development plans in endemic settings

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Vaccine development
Current trials include:

- Vaccine development plans are in line with the recommendations from the GACVS
- Co-administration of single dose SA 14-14-2 with measles vaccine at 8 months (in data analysis)
- Post marketing surveillance in India (ongoing)
- Immunogenicity study in Sri Lanka (planned)
- Evaluation of pre-existing antibodies on immune response
- Review of impact of maternal antibodies on vaccine administered ay 8 months of age
- Evaluating additional trial support with newer candidates in pediatric endemic populations

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Country support
Vaccine introduction:

- Two countries will introduce the SA 14-14-2 this year
- Sri Lanka has plan of introduction in 2007
- New experience will help with lessons learned for next countries introduction
- WHO meeting to create guidelines for introduction
- The SAGE has just made recommendation on the use of JE vaccine
- GAVI indicated that they will request an investment case for JE this year

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India JE vaccine Introduction
A Historic Event

- First “foreign” vaccine introduced into routine immunization in India
- First new vaccine introduced by the Government of India
- First injectable vaccine campaign ever in India

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Vaccine Introduction in India

- Full technical support in areas needed
- File submission and technical support on licensure
- Facilitating communications with manufacturer
- Training of control lab in lot release testing
- Vaccine introduction planning
  - Introduction plan, operational guidelines, training materials, procurement timing
- Vaccine introduction
  - Monitoring and evaluation, AEFI monitoring
- Post licensure studies
  - Immunogenicity, safety, viremia

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Vaccination in India

- Started May 15th, 2006
- Almost 10 million children vaccinated
- 4 states, 11 districts
- First phase of 5 year plan

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Vaccination in India

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Results!

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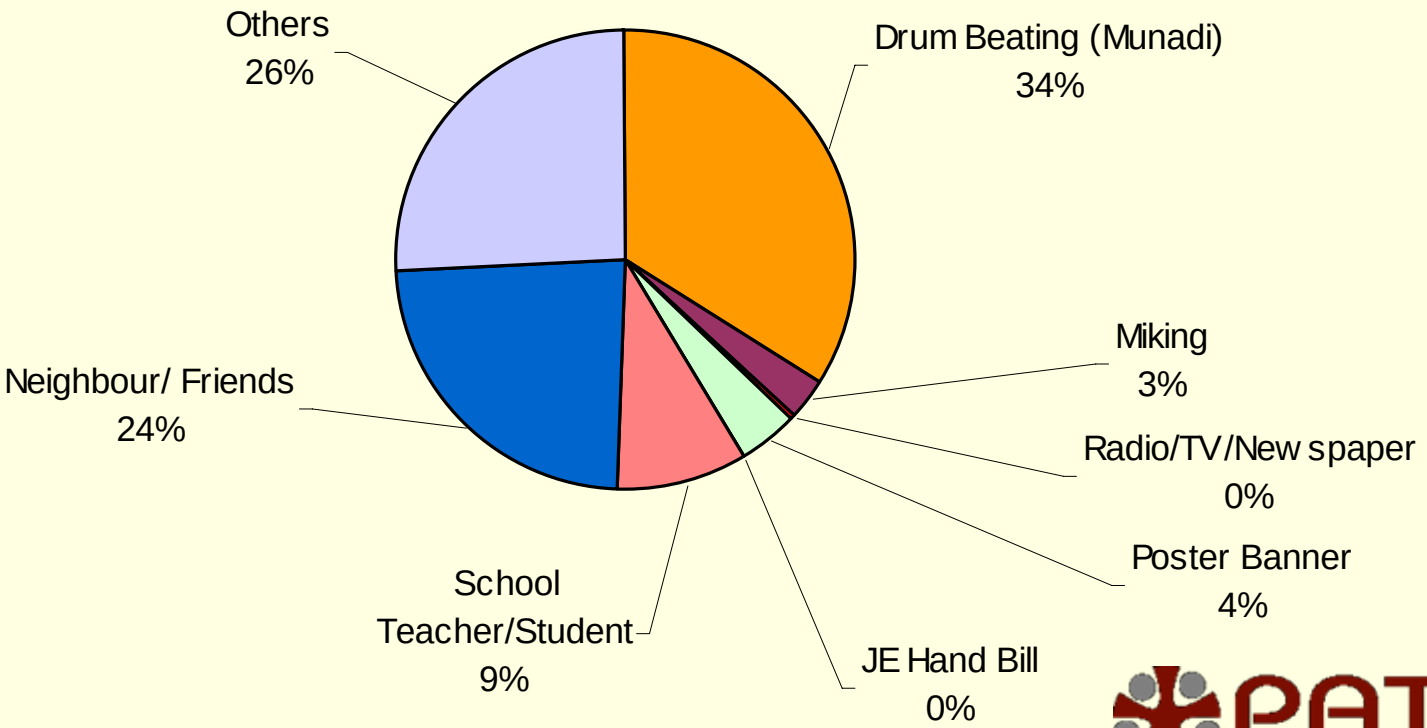
Maharajganj: How care givers came come to know about the campaign

(Source : interview with parents/guardians of child at session site)

Day	15-May	16-May	17-May	18-May	19-May	20-May	21-May	22-May	23-May	24-May	25-May	26-May	27-May	28-May	29-May	Total
Sites Visited	16	31	29	30	37	29	37	36	23	29	25	28	32	28	23	433



Slide from Government of India 2006

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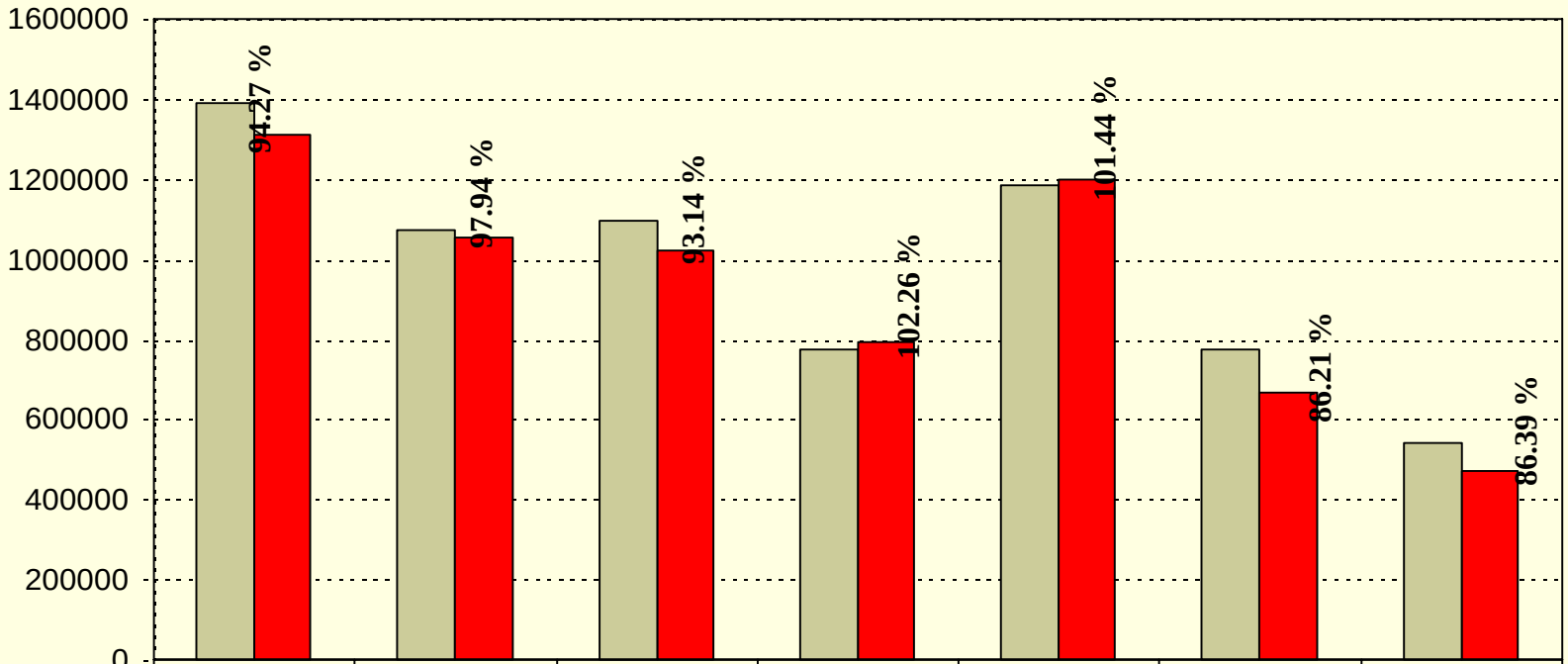
UP – Coverage at a Glance



	Gorakhpur	Deoria	Kushinagar	Maharajganj	Lakhimpur Kheri	Sidhart Nagar	Saint Kabir Nagar
Target (1-15)	1390307	1074219	1095877	776500	1183481	775934	542062
Coverage	1310707	1052079	1020706	794011	1200478	668906	469760

Target: 6838380 Coverage: 6516647 (95.30 %)

Re-activity in the areas where coverage less than 80% for 3-4 days, data not included here.

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Slide from Government of India 2006

General support: Providing key resources to countries and partners

- Pamphlet for parents on JE
- Generic informational posters for JE
- Generic Powerpoint presentations
  - Many topics- JE disease, diagnosis, lumbar puncture, JE vaccine
- AIM e-learning JE vaccine introduction module to be updated this year with a new planning tool
- Immunization training modules
- Web resources at www.jeproject.org

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Providing key resources to countries and partners with WHO

- JE Surveillance Standards
- Encephalitis Clinical Care Guidelines
- JE Vaccine Introduction Guidelines
- New WHO position paper of JE

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Hopefully we will be able to show you more pictures next year from more children being successfully immunized!

Questions or Comments

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